



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Patent Application of:

Morton J. Seligman

Serial No. : 10/061,025

Filed : January 30, 2000

Title : COMPOSITIONS AND METHODS FOR  
TREATING ALLERGIC FUNGAL  
SINUSITIS

: Art Unit : 1616

: Examiner : M. Haghighatian

Assistant Commissioner for Patents  
Washington, D.C. 20231

RESPONSE AND DECLARATION UNDER 37 C.F.R. §1.132 OF  
DR. MORTON J. SELIGMAN

This letter is in response to the Office Action dated December 18, 2002 in the above-captioned application. Claims 1-20 are present in this application.

Accompanying this Application is a Declaration Under 37 C.F.R. §1.132 of Dr. Morton J. Seligman, the inventor of the invention claimed in the captioned Application. This Declaration presents evidence demonstrating that the cited Osbakken Patent Publication does not disclose the claimed invention and that new and unexpected results are achieved by the method and intranasal spray of this invention.

As seen from this evidence presented in this Declaration, Osbakken does not disclose treating the claimed disease, allergic fungal sinusitis and that liquid montelukast delivered in accordance with the teaching of Osbakken is not administered intranasally. The evidence in Dr. Seligman's declaration demonstrates Osbakken's method produces no detectable intranasal delivery of montelukast much less in an effective amount for treating allergic fungal sinusitis i.e., which is an amount at the dosage levels claimed in this Application, i.e., from 0.03 mg to 10 mg per day. As seen from Osbakken reference and the evidence in Dr.

Seligman's declaration , the Osbakken does not discloses intranasal administration but rather administers pharmaceutical agents through an extranasal cloud mist by means of an aerosol nebulizer and not a nose spray.

From the Articles cited in Dr. Seligman's Declaration, infectious fungal sinusitis such as disclosed in the Osbakken Patent Publication is not the same disease as allergic fungal sinusitis which is treated in accordance with the method of this invention. These articles present evidence demonstrating that infectious fungal sinusitis and allergic fungal sinusitis are two different diseases arising from different causes, treated by two different methods and a method for treating one will not necessarily treat the other disease.

In addition, the experiments carried out by Dr. Seligman and reported in this Declaration present evidence which demonstrates that the nebulizer disclosed by Osbakken does not deliver the active ingredient, montelukast, intranasally. As seen from Exhibits 2 and 3, as well as the results reported in Dr. Seligman's Declaration, montelukast when administered at the dosage disclosed by Osbakken, i.e., at 3.5 mg in 3ml of sterile water, did not stain in any manner the filter paper. In fact, these results show that there was no detectable color on the filter paper when montelukast at a dose of 3.5 mg was administered in accordance with the procedure of Osbakken. However, as seen from Exhibit 3, a much lower dose of 0.25 mg applied by means of a nose spray of Dr. Seligman , showed color staining of the filter paper. In fact, as seen from Exhibit 2, color staining is achieved with dosages applied by the Seligman method of 1 mg. The results demonstrate that montelukast when delivered by the method disclosed in Osbakken does not deliver this montelukast intranasally, much less at any dosage level such as disclosed in this invention.

All of the claims have been rejected under 35 U.S.C. §102(e) as being anticipated by the Osbakken Patent Publication. This rejection is respectfully traversed.

The claimed invention in the captioned application is directed to a method for treating patients suffering from allergic fungal sinusitis comprising administering intranasally a montelukast or montelukast type compound. In addition, this invention claims that the

montelukast can be administered to patients intranasally at dosages of from about 0.3 mg to 10 mg per day. The Application also claims intranasal sprays for accomplishing this purpose. The Osbakken Patent Publication does not disclose treating patients suffering from allergic fungal sinusitis. Nor does the Osbakken Patent Publication disclose intranasal sprays for this purpose.

That Osbakken does not disclose treating patients suffering from allergic fungal sinusitis can be seen from the fact that the disease disclosed in Paragraph [0032] of Osbakken is infectious fungal sinusitis not allergic fungal sinusitis. Infectious fungal sinusitis is not allergic fungal sinusitis. In this respect, one need only turn to the Seligman Declaration as well as the Dolan and Marple articles cited therein which demonstrate that infectious fungal sinusitis disclosed by Osbakken is a different disease than allergic fungal sinusitis. These articles demonstrate that each disease has a different clinical presentation and requires different modes of treatment.

Infectious fungal sinusitis is caused by fungi which infect the patient causing the sinusitis condition. On the other hand, allergic fungal sinusitis is caused by allergy conditions which affect the IgE level in the patient. Please note page 1 of the Dolan article which describes the fungal sinusitis is not due to invasive fungi such as those disclosed in the Osbakken reference but rather to an allergic condition which affects the IgE response in a patient. Hence, invasive fungal sinusitis is caused by fungus infection whereas allergic fungal sinusitis is caused by an allergic condition. The same difference is set forth in the Marple publication on page 1007, column 2. As stated in the Marple article on Page 1007, column 2, the allergic IgE caused by this disease remains elevated in the patient even "after prolonged fungal immunotherapy." On page 1009 Marple discloses that patients suffering from allergic fungal sinusitis (AFS) are unresponsive to therapy which is utilized for combating fungus infections. As stated on page 1009, first column

“Patients with AFS are atopic but generally have been unresponsive to antihistamines, intranasal corticosteroids, and prior immunotherapy. The use of systemic corticosteroids may produce some relief of symptoms, but relapse typical follows completion of therapy. In contrast to patients who have invasive fungal sinusitis, patients with AFS are by definition immunocompetent.”

Clearly allergic fungal sinusitis which is treated in accordance with this invention is a different disease from the invasive fungal sinusitis disclosed by Osbakken. As can be seen from the references and Dr. Seligman's Declaration, treatment of one disease does not mean that the same treatment would be effective in treating the other disease. Both diseases have different causes and both diseases have different treatments.

The causes of the sinusitis mentioned in Paragraph [0008] of the Osbakken Patent are through fungal infections and not through an allergic reaction as is the case in allergic fungal sinusitis. Nothing in Osbakken teaches that their method would be useful for treating fungal sinusitis caused by an allergic condition. As seen from the foregoing Seligman Declaration and the references attached thereto, the fact that a therapy is useful for treating infectious fungal sinusitis does not mean that this same therapy is effective in treating allergic fungal sinusitis. Nothing in Osbakken reference would make it obvious to utilize their method for treating allergic fungal sinusitis. In fact there is no disclosure of allergic fungal sinusitis in the Osbakken Publication. The method claims are not anticipated under 35 U.S.C. §102 or rendered obvious under 35 U.S.C. §103.

In addition, Osbakken does not disclose utilizing his method for intranasal administration such as claimed in this Application. The Osbakken Publication discloses many different pharmaceutical agents which can be administered through an extranasal cloud mist by means of an aerosol nebulizer. This is not intranasal administration such as disclosed and claimed in this Application. Nebulization is not intranasal delivery such as by a nose spray or nose drops as claimed in this Application. In addition, as seen by the Declaration of Dr. Seligman, when the specific compound used in the claimed method is formulated and delivered in the manner of Osbakken through an aerosol nebulizer, there is no intranasal delivery of this compound. In the Declaration of Dr. Seligman montelukast was

formulated at a dose of 3.5 mg in 3 ml of sterile water as disclosed in Paragraph [0188] of the Osbakken Publication and cited on page 3 of the Office Action. As seen from the results, there was no staining of the filter paper when this dose of montelukast was used. On the other hand, as seen from Exhibits 2 and 3 of the enclosed Declaration, when lower dosages of montelukast were applied by nasal spray, the red colored montelukast was present on the absorbent filter paper. This indicated that the nasal spray and not the aerosol nebulizer of Osbakken provided intranasal delivery of the montelukast.

Nothing in the Osbakken reference discloses formulating the compounds administered as a intranasal composition or carrying out the method of this invention by intranasal means, much less by means of a nose spray or nose drops. In paragraph [0020] Osbakken teaches away from utilizing intranasal delivery methods such nasal sprays and nasal drops. In this discussion which relates to the Background of the Invention, Osbakken lays out the deficits and deficiencies of utilizing such intranasal means for administering various agents for treating a variety of diseases. In view of this, Osbakken discloses the administration of pharmaceutical agents through an extranasal cloud mist by means of an aerosol nebulizer. Among the hundreds of agents which Osbakken can deliver by his method is included montelukast. The list of compounds that Osbakken discloses that can be administered through an extranasal cloud mist by means of an aerosol nebulizer is enormous. There is no disclosure of any results achieved by the use of the specific compounds claimed in Applicant's method and composition for achieving an effective treatment for allergic fungal sinusitis. Therefore, it is clear that Osbakken does not disclose the method or compositions having the specific compounds in the form for intranasal administration as claimed in this Application. Furthermore, if anything, Osbakken does not render obvious the use of these compounds in a composition for intranasal administration.

In accordance with this invention we have also found that patients suffering from disease states, specifically sinusitis, allergic rhinitis or asthma, who were non-responsive to convention treatment for the disease states are for the most part suffering from allergic fungal sinusitis and that the best way to treat such patients is through intranasal administration of montelukast. This method is disclosed in Claims 7-12. Nothing in the

Osbakken Patent Publication related to treating these types of patients, much less treating any patients intranasally or with montelukast. Clearly, these claims as well as the rest of the claims are neither anticipated nor rendered obvious by the Osbakken Publication.

Based upon the foregoing it is submitted that all of the claims in this Application are in condition for Allowance. A prompt Notice of Allowance is respectfully requested.

### ***Correspondence and Fees***

Please charge Deposit Account No. 03-3839 in the amount of Fifty-Five dollars (\$55.00) to cover the Petition For One Month Extension submitted herewith. No additional fees are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 03-3839 for any underpayment, or to credit any overpayments.

Please address all correspondence to Intellectual Property Docket Administrator, Gibbons, Del Deo, Dolan, Griffinger & Vecchione, One Riverfront Plaza, Newark, NJ 07102-5497. Telephone calls should be made to William H. Epstein at (973) 596-4607 or (973) 596-4500 and fax communications should be sent directly to him at (973) 639-6397 or (973) 596-0545.

Respectfully submitted.



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